tions of clonidine. *In* Onesti G, Kim KE, Moyer JH (Eds): Hypertension: Mechanisms and Management. New York, Grune and Stratton. 1973, pp 369-380

7. Kobinger W, Walland A: Investigations into the mechanism of the hypotensive effect of 2-(2,6-dichlorphenylamino)-2-Imidazoline-HCL. Europ J Pharmacol 2:155-162, 1967

8. Haeusler G, Finch L, Thoenen H: Central adrenergic neurones and the initiation and development of experimental hypertension. Experientia 28:1200-1203, 1972

9. Finch L: The central hypotensive action of clonidine and BAY 1470 in cats and rats. Clin Sci Mol Med (Suppl) 148:273s-276s, 1975

10. Onesti G, Paz-Martinez V, Kim KE, et al: Effect of clonidine on renin release. *In* Onesti G, Kim KE, Moyer JH (Eds): Hypertension: Mechanisms and Management. New York, Grune and Stratton. 1973, pp 405-409

11. Weber MA, Case DB, Baer L, et al: Renin and aldosterone suppression in the antihypertensive action of clonidine. Am J Cardiol 28:825-826, 1976

12. Hansson L, Hunyor SN, Julius S, et al: Blood pressure crisis following withdrawal of clonidine (Catapres, Catapresan), with special reference to arterial and urinary catecholamine levels, and suggestions for acute management. Am Heart J 85:605-610, 1973

13. Hunyor SN, Hansson L, Harrison TS, et al: Effects of clonidine withdrawal: possible mechanisms and suggestions for management. Br Med J 2:209-211, 1973

14. Reid JL, Wing LM, Dargie HJ, et al: Clonidine withdrawal in hypertension—Changes in blood-pressure and plasma and urinary noradrenaline. Lancet 1(8023):1171-1174, 1977

15. Strauss FG, Franklin SS, Lewin AJ, et al: Withdrawal of antihypertensive therapy—Hypertensive crisis in renovascular hypertension. JAMA 238:1734-1736, Oct 17, 1977

16. Hoobler SW, Kashima T: Central nervous system actions of clonidine in hypertension. Mayo Clinc Proc 52:395-398, 1977

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Thrombocytopenia Associated With Intravenous Heroin Abuse

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ALTHOUGH multiple medical complications are associated with the intravenous injection of illicit drugs,[1-3] thrombocytopenia has only recently been reported.[4] In only two years we have encountered four cases of intravenous heroin abuse in which patients presented with blood loss due to severe thrombocytopenia. In only one patient was there evidence of concurrent infection. A representative case follows.

Reports of Cases

A 19-year-old man (Case 1, Table 1) was admitted to University Hospital with a ten-day history of easy bruising, blood loss from mucous membranes, melena and hematuria. He had intermittently used heroin intravenously and cocaine for about two years. Results of physical examination showed a temperature of 38.2°C (100.8°F), purpura, petechiae and a palpable spleen tip. Laboratory data included a normal leukocyte count and a platelet count of 1,000 per cu mm. The patient's fever abated in one day without therapy. Administration of prednisone, 100 mg per day, was begun and the platelet count returned to normal levels in ten days. A bone marrow biopsy showed an increase in megakaryocytes and normal cellularity. Prednisone was tapered to 60 mg per day over one week, but thrombocytopenia returned (Figure 1). The patient said he no longer was abusing drugs. Reinstitution of prednisone therapy at 100 mg per day resulted in a return of the platelet count to normal levels in seven days; however, thrombocytopenia recurred during administration of steroids. Splenectomy was done and prednisone again tapered. The platelet count was 276,000 per cu mm when the patient was seen in a follow-up examination 18 months later.

A summary of the clinical characteristics of the four patients we saw is shown in Table 1. As in most cases of drug abuse the patients were young and had used multiple drugs for several years.[1] In case 4 concomitant staphylococcus sepsis was present, but findings on examination for disseminated intravascular coagulation were normal. Although thrombocytopenia may be present in patients with acute bacterial endocarditis, it is an unusual presenting manifestation of this disorder.[5]

In one patient (Case 3) there was a positive radioimmunoassay for hepatitis B antigen but all other liver function tests gave normal findings at the time of presentation. Five weeks later, thrombocytopenia recurred while the patient was on a regimen of 20 mg of prednisone per day. The patient denied intravenous abuse of drugs but admitted to excess intake of alcohol. Findings on

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liver function tests were elevated at the time of relapse. Prednisone therapy had been started again, at a dosage of 100 mg per day, and the platelet count was rising when the patient left the hospital against medical advice.

In all four of the patients bone marrow studies had been done on admission and no evidence of toxic alcohol effects was found.

Table 2 shows the responses to treatment. In all cases prednisone therapy, 80 to 100 mg given orally per day, was begun on admission and continued until the platelet count rose to normal. The platelet count increased to 100,000 per cu mm in all patients receiving initial steroid therapy. In two, relapses occurred when administration of steroids was tapered, but the platelet count increased rapidly to normal levels with administration of higher doses of steroids.

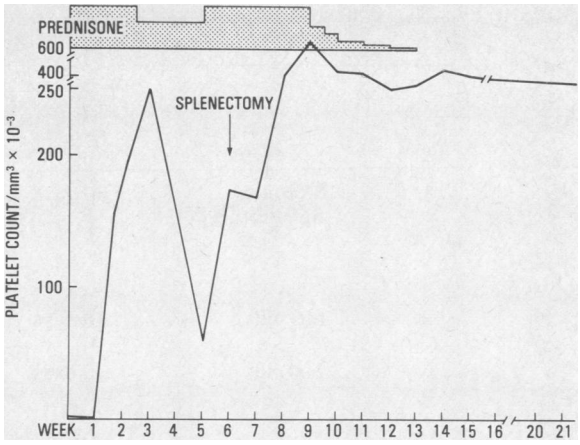

Figure 1.—Peripheral blood platelet counts and clinical course in patient 1 with heroin-associated thrombocytopenia.

Discussion

Adams and co-workers have recently reported five cases of thrombocytopenia associated with the use of heroin.[4] These cases differ in some respects from the four we encountered. Three of their patients were seen in four days and these authors postulated that there had been a common exposure to some toxic element, possibly "brown" heroin. Our four patients were seen during a period of two years. Although "brown" heroin has been in common use in San Diego during this time, we cannot implicate it as a common factor in our four cases.

The cause of thrombocytopenia in these cases is unclear. Most intravenous drug abusers are constantly exposed to multiple illicit drugs, adulterants (including quinine),[1] and bacterial and viral antigens that might be associated with thrombocytopenia. The clinical course in at least two of our patients resembled autoimmune thrombocytopenia;[6] in both of these patients relapse occurred during a period of steroid therapy. One patient may have benefited from splenectomy and has a normal platelet count after all therapy has been stopped. Whether the two relapses were due to a continuing immune response or to resumption of drug abuse is unknown. Other authors[8] have noted immunologic disturbances in heroin abusers, but the relationship of these observations to the thrombocytopenia observed by Adams and by us remains conjectural. The recurrent exposure to illicit drugs, however, can

TABLE 1.—*Characteristics of Intravenous Drug Abusers With Thrombocytopenia*

Case	*Age*	*Presenting Complaint*	*Duration of Drug Abuse*	*Drugs*	*Splenomegaly*	*Bone Marrow Megakaryocytes*
1	19	Epistaxis Purpura Melena Hematuria	Two years	Heroin Cocaine	Tip palpable	Increased
2	27	Gum bleeding Petechiae	Ten years	Heroin Alcohol	Absent	Increased
3	25	Ecchymosis	Seven years	Heroin Alcohol Propoxyphene hydrochloride (Darvon) Methaqualone (Quaalude) Chloral hydrate	Absent	Increased
4	29	Gum bleeding Purpura	Eight years	Heroin Alcohol Meperidine hydrochloride (Demerol) Diazepam (Valium) Codeine	Absent	Increased

TABLE 2.—*Response to Therapy in Patients With Thrombocytopenia*

Case	*Treatment*	*Time to Reach a Platelet Count >100,000 per cu mm on Initial Steroid Therapy*	*Outcome*
1	Steroids Splenectomy	10 days	Relapsed when administration of steroids was tapered; responded to readministration of steroids in seven days; platelet count now normal 18 months after splenectomy; all medications stopped
2	Steroids	10 days	Platelet count normal one month after presentation; all medications stopped
3	Steroids	6 days	Responded initially to steroid therapy but relapse occurred when steroid therapy was discontinued; responded to readministration of steroids within 13 days, lost to follow up
4	Steroids	30 days	Platelet count normal after 24 months; all medications stopped

never be ruled out with certainty in cases of drug abuse.

Enough similarities exist between our patients and those in the report by Adams to indicate that the association between heroin abuse and thrombocytopenia is a real one. In our cases and those of Adams there was a sudden onset of mucous membrane and cutaneous blood loss. Little evidence of concomitant infection was present in three of our four patients and in those previously reported. In three of our four cases, and in four of five of Adams' cases, platelet counts returned to normal within ten days after steroid therapy was started. Adams noted relapses in three of five patients when administration of steroids was tapered, and relapse occurred in two of our four within five weeks after initial diagnosis, while high doses of prednisone were still being given. Whether protracted steroid therapy—as in immune thrombocytopenia—or short-term therapy—as in drug-induced thrombocytopenia—should be used in these cases is unknown. Thrombocytopenia, however, should be added to the list of medical complications associated with intravenous heroin abuse.

Summary

In a period of two years four patients were seen with severe thrombocytopenia associated with intervenous heroin abuse. All were young, all had abused multiple drugs and all presented with mucocutaneous bleeding. In three of the patients there was an initial response to steroid therapy with a rise in platelet count to the normal range within ten days. In two of these patients, recurrent thrombocytopenia occurred when steroid therapy was discontinued, indicating a continuing process. Both denied continued intravenous abuse of drugs. In two the platelet count is now normal after all medication has been stopped and in a third the platelet count is normal after all medication has been stopped and after splenectomy. The cause of this complication is unclear, but thrombocytopenia should be added to the growing list of medical complications associated with intravenous abuse of heroin.

REFERENCES

1. Sapira JO: The narcotic addict as a medical patient. Am J Med 45:555-588, 1968

2. Richter RW (Ed): Medical Complications of Drug Abuse. San Francisco, Harper and Row, 1975

3. Louria D: The medical complications of drug abuse, *In* Glatt MM (Ed): Drug Dependence—Current Problems and Issues. Baltimore, University Park Press, 1977, pp 149-165

4. Adams WH, Rufo RA, Talarico L, et al: Thrombocytopenia and intravenous heroin use. Ann Intern Med 89:207-211, 1978

5. Kaye D: Changes in the spectrum, diagnosis and management of bacterial and fungal endocarditis. Med Clin N Am 57:941-957, 1973

6. Aster RH: Thrombocytopenia due to enhanced platelet destruction, *In* Williams WJ, Bentler E, Erslev AJ, et al (Eds): Hematology. San Francisco, McGraw-Hill, pp 1342-1359, 1977

7. Brown SM, Stennel B, Taub RN, et al: Immunologic dysfunction in heroin addicts. Arch Intern Med 134:1001-1006, 1974

8. Husby G, Pierce PE, Williams RC Jr: Smooth muscle antibody in heroin addicts. Ann Intern Med 83:801-805, 1975